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09/937,103	07/05/2002	Sandrine Lentsch Graf	01-1081	4719

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EXAMINER	
FORD, VANESSA L	

ART UNIT	PAPER NUMBER
1645	7

DATE MAILED: 12/12/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/937,103	Applicant(s) GRAF ET AL.	
	Examiner Vanessa L. Ford	Art Unit 1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 July 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Specification Objections

1. The claims are objected because of the following informalities: The names of genus and species of organisms should be underlined or italicized. See page 3. Applicant is asked to review the specification for these types of informalities and correction is required.

2. The use of the trademarks, for example page 8 has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks. 608.01.

Claim Objections

3. The claims are objected to because of the following informalities: The names of genus and species of organisms should be underlined or italicized. See claim 2. Correction is required.

4. Claim 9 is objected to because of the following informalities: Claim 9 recites "The method" and should recite "A method" because it is an independent claim. Correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 9-10 are rejected under 35 USC 112 second paragraph for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims recite "a method", what are the steps in the claimed method? There are no method steps positively recited in the claimed method. It is unclear as to what steps in the claimed method Applicant is referring? Clarification is required.

Claim Rejection - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

6. Claims 1-4 are rejected under 35 U.S.C. 102(e) as anticipated by LaPosta et al *(U.S. 6,306,4004 published October 23, 2001).*

Claims 1-4 are drawn to a liquid vaccine composition comprising at least one antigen consisting of a polysaccharide bound to a carrier protein, wherein it additionally comprises trehalose.

LaPosta et al teach a liquid vaccine composition comprising a polysaccharide covalently bound to a protein (column 4, lines 60-65). LaPosta et al teach that sugars such as trehalose may be added to the vaccine composition to prevent aggregation (i.e. stabilize) of the vaccine composition (column 3, lines 10-26). LaPosta et al anticipates the claimed invention. LaPosta et al teach suitable antigens used in the vaccine include antigens from *Haemophilus influenzae, Neisseria meningitidis* and *Streptococcus pneumoniae*, Group A *Streptococcus* and Group B *Streptococcus* (column 4, lines 25-64). LaPosta et al teach that the antigens of the invention, for example, bacterial capsular polysaccharide or a fragment thereof is chemically linked to a protein carrier molecule in order to enhance immunogenicity (column 4, lines 60-64). LaPosta, et al anticipates the claimed invention.

Since the Office does not have the facilities for examining and comparing applicant's vaccine and the vaccine of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the vaccine does not possess the same material structural and

functional characteristics of the claimed vaccine). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Claim Rejection - 35 USC § 102/103

7. Claims 9-10 are rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious LaPosta et al *(U.S. 6,306,4004 published October 23, 2001).*

Claim 9-10 are drawn to a method of stabilizing a liquid vaccine composition comprising at least one antigen consisting of a polysaccharide bound to a carrier protein, wherein it consists in adding trehalose to the vaccine composition.

LaPosta et al teach a method of stabilizing a liquid vaccine composition comprising at least one antigen consisting of a polysaccharide bound to a carrier protein, wherein it consists in adding trehalose to the vaccine composition by teaching that sugars such as trehalose may be added to the vaccine composition to prevent aggregation (i.e. stabilize) of the vaccine composition (column 3, lines 10-26). LaPosta et al teach suitable antigens used in the vaccine include antigens from *Haemophilus influenzae, Neisseria meningitidis* and *Streptococcus pneumoniae*, Group A *Streptococcus* and Group B *Streptococcus* (column 4, lines 25-64). LaPosta et al teach that the antigens of the invention, for example, bacterial capsular polysaccharide or a fragment thereof is chemically linked to a protein carrier molecule in order to enhance immunogenicity (column 4, lines 60-64). The method of LaPosta et al is the same as the claimed method. LaPosta et al do not specifically teach the claimed quantities of

trehalose added to the vaccine compositions. However, in the alterative, it would have been obvious at the time the invention was made to the add specific quantities of trehalose to the vaccine compositions of LaPosta et al because the addition of specific quantities of trehalose would be well within the level of skilled in the art and would be a matter of optimizing experimental parameters. Additionally, LaPosta et al teach that the addition of a sugar such as trehalose to the vaccine composition prior to freezing or lyophilization provides a composition which after freezing can be thawed to afford an aqueous colloidal suspension without further sonication of or alternatively after lyophilization can be reconstituted with a suitable aqueous diluent without further sonication (column 3, lines 10-24). It would be expected barring evidence to the contrary that vaccine comprising trehalose would retain their stability in long-term storage.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 1-8 are rejected under 35 U.S.C. 103(a) as unpatentable over Anderson et al *(U.S. Patent No. 5,097, 020, published March 17, 1992)* in view of Roser *(WO 95/33488, published December 14, 1995).*

Claims 1-8 are drawn to a liquid vaccine composition comprising at least one antigen consisting of a polysaccharide bound to a carrier protein wherein it additionally comprises trehalose.

Anderson et al teach vaccine comprising covalent attachment of capsular polymer fragment derived from bacterial capsular polymers to bacterial toxoids (column 2, lines 58-64). Anderson et al teach that suitable carrier proteins of the inventions include diphtheria and tetanus toxoids (columns 5, lines 29-36). Anderson et al teach that vaccine of the invention include vaccines against systemic infections caused by the pathogens *Haemophilus influenzae* type b, *E. coli*, pneumococcus, meningococcus, streptococcus and pseudomonas (column 6, lines 59-65). Anderson et al teach that the regulation of any reaction parameter, e.g. time, temperature, pH, etc. which affects the reactivity or rate of reaction will alter the final composition and structure of the conjugate (column 4, lines 45-49). Anderson et al teach that the vaccines of the invention have been lyophilized (column 18, lines 35-40). Anderson et al teach that the conjugates of the invention appear to convert into macromolecular aggregates after preparation (column 13, lines 67-68 and column 14, lines 1-2).

Anderson et al do not teach the use of trehalose.

Roser et al teach the use of trehalose as a means of protecting substances such as vaccines from aggregation (see the Title and the Abstract). Roser et al teach that the addition of trehalose to biologically active substances can reduce aggregation during dehydration and rehydration (page 4). Roser et al teach that the addition of trehalose prevents the formation of all multimeric forms of the substance (page 5).

Roser el al teach the addition of trehalose in the amount of about 1% to 50% more preferably about 5% to 25% to biologically active substances (page 7). Roser et al teach that material dried in the presence of trehalose, when resuspended produces a smooth and single particulate suspension (page 9).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to add the trehalose as taught by Roser et al to the immunogenic conjugate vaccines of Anderson et al because Roser et al teach the use of trehalose as a means of protecting substances such as vaccines from aggregation and Roser et al also teach that the addition of trehalose prevents the formation of all multimeric forms of the substance. It would be expected barring evidence to the contrary that vaccine comprising trehalose would retain their stability in long-term storage.

Status of the Claims

9. No claims allowed.

Conclusion

10. Any inquiry of the general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308–0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Office Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for the Group 1600 is (703) 308-4242.

Any inquiry concerning this communication from the examiner should be directed to Vanessa L. Ford, whose telephone number is (703) 308-4735. The examiner can normally be reached on Monday – Friday from 9:30 AM to 6:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached at (703) 308–3909.

Vanessa L. Ford
Biotechnology Patent Examiner
November 24, 2003

MARK NAVARRO
PRIMARY EXAMINER